REMARKS

Status of the Claims

Claims 1-3 and 5-7 are currently pending and under consideration.

Claim 1 is presently amended. Features of the internal control template were added to the claim: "at least one internal control template comprising a sequence with binding sites complementary to the at least first set of amplification primers further capable of amplifying the internal control template,...". Support for this amendment can be found throughout the specification as filed, for example on page 19 line 32 – page 20 lines 1-5, again on page 20 lines 25-31 and also in the Example.

Further amendments were made to claim 1 step bca): "...said hybridization being indicative of the presence of said pathogic organism and at least the genus of said pathogenic organism...". Support for this amendment can be found throughout the specification as filed, for example in the Examples section.

No new matter is added by these amendments.

Double Patenting

The Examiner has provisionally rejected claim 1 on the grounds of nonstatutory obviousness-type double patenting over claim 1 of copending Application No. 10/532,319.

Application No. 10/532,319 has issued as US 7,718,361 on May 18, 2010. Accordingly, Applicants submit if these provisional rejections are the only outstanding rejections, and the present claims are otherwise allowable, Applicants will file a Terminal Disclaimer.

Claim Interpretation

Regarding the internal control template, the Examiner has noted that she has given the term the broadest reasonable interpretation, reading on templates with and without shared primer sites. (Action page 5) Solely to facilitate prosecution, applicants have amended claim 1 to provide further limitations and clarification on the design and structure of the internal control template, requiring the internal control template to have shared primer sites:

> bb) at least one internal control template comprising a sequence with binding sites complementary to the at least first set of amplification primers further capable of amplifying the internal control template,

Applicants assert that claim 1 as presently amended reads upon control templates that are co-amplified along with the target using shared primer sites in the target and control templates, and claim 1 as presently amended does not read upon amplification using different, non-shared primers.

Claim Rejections - 35 USC §103

The Examiner has rejected claims 1-3 and 7, under 35 USC 103(a) as being unpatentable over Edwards et al in view of Forsman, Bergeron, Bergeron '564, Kunsch '98, Kunsch '97, Naimi, Lowe and Buck. The Examiner repeats the rejections from the prior Action, asserting in part that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teaching of Edwards in light of the other cited prior art to arrive at the claimed invention with a reasonable expectation for success. (Action pages 6-20)

Solely to facilitate prosecution, Applicants have amended claim 1 step bca) to clarify that the hybridization is indicative of the presence of the pathogenic organism AND the genus of the organism. Further, Applicants respectfully traverse the rejections.

The Examiner cites Edwards Figure 1 as teaching claim 1 step bca). (Action page 7) Applicants repeat the assertions from the previous response that Figure 1 does not teach monitoring hybridization of each of said hybridization reagents at a pre-selected temperature, said hybridization being indicative of the presence of said pathogic organism and of at least the genus of said pathogenic organism present in the sample as required by instant claim 1 step bca).

Step bca) requires determining if hybridization of a hybridization reagent (probe) occurred at a pre-selected temperature; this event is determined by measuring the cycle number at which a positive amplification signal could be detected. For example, refer to the Examples in the specification as filed, specifically the Results section where a table of Cp values (cycle number where a positive amplification signal could be detected) is provided. The Cp value was determined by the method of step bca). In addition to the detection of a positive hybridization event, the detection of the amplification signal determines at least the genus of the pathogenic organism. These requirements are all provided by claim 1 step bca).

The Examiner has not cited any evidence in Edwards providing the methods as required by Applicants' step bca) as detailed above. The Examiner refers to Edwards p. 3048, col. 1: "fluorescence readings were taken after annealing at 55°C for 1 s" which is followed by melt curve analysis. The Examiner then notes that "the hold at the first temperature before the melt meets the limitation of the claim". (Action page 7) Applicants assert that the Examiner has taken this citation of the 55°C for 1 s step out of context of the full methods as taught in Edwards. Edwards teaches the following LightCyler parameters:

1 cycle:	94°C	5 s
40 cycles:	94°C	0 s
	55°C	**1 s**
	60°C	**15 s**
	74°C	**10 s**

Applicants note that Edwards teaches 3 temperatures (55, 60 and 74) at which fluorescence could be measured. The exact temperature for Edwards' "reading" is not provided.

Further, in the Results section, Edwards teaches: "The probes were all designed to have an annealing temperature at least 5°C higher than that of the primers." Knowing this information, one skilled in the art would appreciate that Edwards teaches that the primers have an annealing temperature at 55°C, and the probes have an annealing temperature of *at least* 60°C. The monitoring hybridization of each of said hybridization reagents, as required by claim 1 step bca), is the determination if hybridization of the hybridization reagents (i.e. probes) has occurred. It is not possible for the fluorescence readings to be taken at 55°C because the probes have an annealing temperature *at least* 5°C higher. There would not be hybridization of probes present until 60°C or higher, therefore there would be no fluorescence at 55°C to monitor. Edwards teaches that readings are taken *after, not at* annealing at 55°C. There is no instruction in Edwards to take a reading at a single specific pre-determined defined temperature.

Further, there is no data presented in Edwards resulting from this "fluorescent reading", and there is no teaching in Edwards on what significance this "fluorescent reading" provides relative to genus determination. There is no data or teaching provided in Edwards analogous to Applicant's Cp value measurements as provided in the Examples. Edwards does provide teachings on their "hybridization reagents" (i.e. Bioprobes) by way of melting curve analysis only. Therefore the

Examiner has erred in citing the 55°C step as the pre-selected temperature meeting the limitations of claim 1 step bca).

The Examiner also cites Edwards Figure 1 as providing hybridization of the probes at pre-selected temperatures. (Action page 7) Applicants assert that the Examiner is in error in citing Edwards Figure 1 as teaching claim 1 step bca). Edwards Figure 1 provides only a melting temperature profile where each probe is monitored at *many different* temperatures, not at the singular "pre-selected temperature" as required by the instant claims. Claim 1 requires all amplification and detection reagents in one reaction vessel, therefore all reagents are subject to the same pre-selected temperature. The data of Figure 1 is generated from a temperature range from 40°C to 95°C; no data is provided in Figure 1 of the detection of hybridization at a single pre-selected temperature.

Both the monitoring of a hybridization event "bca" AND the monitoring of temperature dependence "bcb" (melting profile) are required to achieve the methods of instant claim 1. Edwards provides only one of these steps. Edwards does not teach or suggest the method as provided by instant claim 1 that requires both steps bca) and bcb) providing both genus and species information in a single reaction vessel.

Edwards does not teach or suggest a method comprising both a genus and a species determination as provided in the instant invention. Edwards provides a direct species-only determination by melting curve analysis without any proceeding genus determination; in fact, Edwards only provides teachings on one genus – Staphylococcus. When samples comprising multiple genera are tested in the methods provided by Edwards without a genus determination, it is possible that the different genera could result in similar melting temperature profiles. For example,

in the methods of Edwards, testing of a sample comprising both E. coli and S. aureus together in one reaction vessel may give a single peak at one melting temperature, leading to ambiguous results. Edwards does not provide for testing of such a sample with multiple genera. The methods of the instant invention do provide for the determination of multiple genera and species. This separate genus and species identification enables one of skill in the art to determine in a single reaction vessel precisely the genus and species (or, multiple genera and species) that may be present in a clinical sample. The methods provided in instant claim 1 allow for simultaneously detecting and identifying a broad range of pathogenic organisms of interest.

Additionally, Applicants have amended claim 1 to clarify the required limitations of the internal control template. Applicants assert that claim 1 as presently amended reads upon control templates that are co-amplified along with the target using shared primer sites in the target and control templates, and claim 1 as presently amended does not read upon amplification using different, non-shared primers. The Examiner has not cited any art related to the use of an internal control template as required by claim 1 step bb).

For the reasons provided above, Applicants assert that Edwards does not teach all of the required claim elements of claim 1 or its dependents. None of the other art cited by the Examiner in combination with Edwards teaches or suggests the method of claim 1 or its dependents. Applicants respectfully submit that the Examiner has not provided a *prima facie* case of obviousness because the combination of Edwards, Forsman, Bergeron, Bergeron '564, Kunsch '98, Kunsch '97, Naimi, Lowe and Buck does not anticipate each every limitation set forth in the claims.

The Examiner has rejected claim 5 under 35 USC 103(a) as being unpatentable over Edwards et al in view of Forsman, Bergeron, Bergeron '564, Kunsch '98, Kunsch '97, Naimi, Lowe and Buck as applied to claims 1-3 and 7, and further in view of Jannes. (Action page 18). Further, the Examiner has rejected claim 6 under 35 USC 103(a) as being unpatentable over Edwards et al in view of Forsman, Bergeron, Bergeron '564, Kunsch '98, Kunsch '97, Naimi, Lowe and Buck as applied to claims 1-3 and 7, and further in view of Loeffler. (Action page 19).

Applicants assert that neither Jannes nor Loeffler teach or suggest the claim elements missing from Edwards as detailed above, requiring both steps bca) and bcb) providing both genus and species information in a single reaction vessel. Neither Jannes nor Loeffler teach or suggest the use of an internal control template as required in step bb). Therefore the combination of the cited art does not anticipate each and every limitation set forth in the claims. Thus, the Examiner has not established a *prima facie* case of obviousness.

For the reasons provided above Applicants respectfully request reconsideration and withdrawal of all of the §103 rejections of independent claim 1 and all other claims depending from claim 1.

CONCLUSION

Applicants respectfully request entry of the present amendments and remarks. In view of the above, Applicants believe all claims now pending in this Application are in condition for allowance. If the Examiner believes that a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-730-8566.

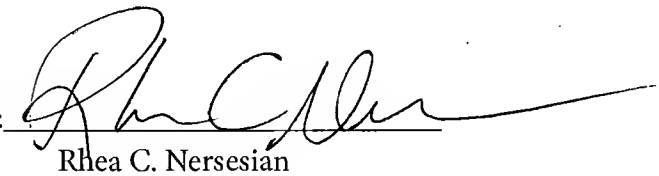
Applicants respectfully request a 1-month extension of time to respond to the Office Action notification date October 12, 2010. The response date was January 12, 2011; with the granting of this request, the response time is re-set to Monday February 14, 2011 (February 12, 2011 is a Saturday).

The commissioner is hereby authorized to charge the amount of $ 130, the fee due under 37 CFR §1.17(a)(1) to Deposit Account No. 50-0812. Please grant any additional extensions of time that may be required to enter this amendment and charge any additional fees or credit any overpayments to Deposit Account No. 50-0812.

Please direct all future correspondences to: Customer No. 22829.

Respectfully submitted,

Date: February 14, 2011

By: 

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